Complete Summary

GUIDELINE TITLE

The role of taxanes in first-line therapy of advanced non-small cell lung cancer.

BIBLIOGRAPHIC SOURCE(S)

Lung Cancer Disease Site Group. Chu Q, Vincent M, Logan D, Mackay JA, Evans WK. The role of taxanes in first-line therapy of advanced non-small cell lung cancer [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2004 Jul 20. 49 p. (Practice guideline report; no. 7-7-1). [65 references]

GUIDELINE STATUS

This is the current release of the guideline.

The FULL REPORT, initially the full original Guideline or Evidence Summary, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the Cancer Care Ontario Web site for details on any new evidence that has emerged and implications to the guidelines.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Advanced non-small cell lung cancer

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Oncology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To evaluate the role for taxanes (paclitaxel or docetaxel), alone or in combination with other chemotherapy agents, in the first-line treatment of advanced non-small cell lung cancer

TARGET POPULATION

Patients with advanced non-small cell lung cancer who are candidates for palliative, first-line chemotherapy

INTERVENTIONS AND PRACTICES CONSIDERED

Treatment

1. Paclitaxel/docetaxel as single agents
2. Paclitaxel/docetaxel-platinum doublets
3. Non-platinum-based paclitaxel/docetaxel doublets
4. Paclitaxel/docetaxel-based triplet combination chemotherapy

MAJOR OUTCOMES CONSIDERED

- Survival
- Response rate
- Toxicity
- Quality of life

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

A systematic search of MEDLINE (Ovid) (1985 through January 2004), EMBASE (Ovid) (1980 through 2004, week 34), CANCERLIT (Ovid) (1985 through October

2002), and the Cochrane Library (2004, Issue 3) databases was carried out. The subject headings "carcinoma, non-small-cell lung" and "paclitaxel" were combined with each of the following phrases used as text words: "non small cell lung", "paclitaxel", "taxol", "docetaxel", and "taxotere". These terms were then combined with the search terms for the following publication types and study designs: practice guidelines, meta-analyses, systematic reviews, and randomized controlled trials. In addition, conference proceedings of the American Society of Clinical Oncology (ASCO, 1996 through 2003), the European Society for Medical Oncology (ESMO, 2002), and the European Cancer Conference (ECCO, 2003) were searched for abstracts of relevant trials. The Canadian Medical Association Infobase (http://mdm.ca/cpgsnew/cpgs/index.asp) and the National Guideline Clearinghouse (http://www.guideline.gov) were also searched for existing, evidence-based practice guidelines. Relevant articles and abstracts were selected and reviewed by three members of the Lung Disease Site Group (DSG), and the reference lists from these sources were searched for additional trials, as were the reference lists from relevant review articles.

Inclusion Criteria

Articles were selected for inclusion in this overview of the evidence if they were:

1. Randomized trials comparing: a) the effect of paclitaxel, alone or in combination, with other chemotherapy regimens or best supportive care (BSC) for patients with advanced non-small cell lung cancer (NSCLC); or b) the effect of docetaxel, alone or in combination, with other chemotherapy regimens or best supportive care for patients with advanced NSCLC; or c) different doses or schedules of paclitaxel or docetaxel.
2. Trials evaluating paclitaxel or docetaxel as first-line chemotherapy for advanced NSCLC. The use of chemotherapy in a neoadjuvant setting at least one year prior to the evaluation of paclitaxel or docetaxel was not considered as prior therapy. See the Disease Site Group Consensus Process section of this report
3. Trials in which at least one of the following outcomes was reported by treatment group: survival, response, toxicity, or quality of life (QOL)
4. Trials that were fully published or reported in abstract form at a major scientific meeting such as American Society of Clinical Oncology

Exclusion Criteria

1. Letters and editorials reporting trial results
2. Papers published in a language other than English
3. Abstracts reporting preliminary data

NUMBER OF SOURCE DOCUMENTS

Twenty-four randomized trials involving paclitaxel and 12 involving docetaxel, either as single agents or in combination with other chemotherapeutic agents, were included in the development of this practice guideline report.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

A meta-analysis of the data was not undertaken due to the heterogeneous nature of the chemotherapy regimens involved and the limited number of similar comparisons reported.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The challenge of comparing the results of trials involving taxane-platinum combination regimens with other new-agent combination regimens was noted by a number of Disease Site Group (DSG) members. In one trial, paclitaxel-cisplatin achieved similar survival to paclitaxel-carboplatin and docetaxel-cisplatin. Two other trials found paclitaxel-carboplatin to have similar efficacy to vinorelbine-cisplatin. It may then be expected that the efficacy of paclitaxel-cisplatin and docetaxel-cisplatin would be similar to that of vinorelbine-cisplatin. However, an indirect comparison of different treatment regimens across trials is not appropriate and may be misleading because other differences between trials (e.g., the composition of the patient population) may contribute to any apparent treatment differences. In addition, some trials accounted for the impact of multiple comparisons in their assessment of significance while others did not, and some trials reported unadjusted analyses while others adjusted for prognostic factors, effectively accounting for potential between-group differences in those factors. These methodological issues continue to be controversial. A direct comparison of cisplatin combined with either vinorelbine or docetaxel in one trial detected a modest but statistically non-significant survival advantage for the latter regimen, although the proportion of patients with stage IV disease in this trial was lower than that in other trials involving comparisons between new-agent combination regimens (67% versus 79% to 89%).

The Lung DSG discussed the definition of chemo-na•ve patients. It was decided that chemo-na•ve patients could also include patients who had received chemotherapy with either radical radiation and/or surgery, with curative intent, at least 12 months prior to the development of recurrent or metastatic disease.

The role of paclitaxel infusion durations was also discussed. It was concluded that most infusions would be three hours although the evidence from clinical trials has

not demonstrated the superiority of one schedule over another. The rationale for choosing the three-hour schedule is a practical one that allows administration as an outpatient rather than as an in-patient, which is required for 24-hour infusions.

With regard to weekly dosing, the Lung DSG felt that there is currently insufficient data on this issue to inform decision-making for patients with advanced lung cancer requiring chemotherapy.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Practitioner feedback was obtained through a mailed survey of 106 practitioners in Ontario (35 medical oncologists, 23 radiation oncologists, 27 surgeons, 20 respirologists, and one hematologist). The survey consisted of items evaluating the methods, results, and interpretive summary used to inform the draft recommendations and whether the draft recommendations above should be approved as a practice guideline. Written comments were invited. The practitioner feedback survey was mailed out on September 26, 2003. Follow-up reminders were sent at two weeks (post card) and four weeks (complete package mailed again). The Lung Disease Site Group (DSG) reviewed the results of the survey.

Final approval of the practice guideline report is obtained from the Practice Guidelines Coordinating Committee (PGCC).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

- The combination of paclitaxel (Taxol®) or docetaxel (Taxotere®) with cisplatin can be recommended as one of a number of chemotherapy options in the first-line therapy of patients with advanced non-small cell lung cancer and a good performance status.
- In patients who have a contraindication to the use of cisplatin or who experience serious toxicity from cisplatin and/or refuse treatment with cisplatin, the substitution of carboplatin for cisplatin in a taxane doublet regimen may be a reasonable treatment option.

- The most commonly used taxane-based regimens in North America have been administered on a three-weekly schedule and include: i) docetaxel 75 mg/m^2 with cisplatin 75 mg/m^2, ii) paclitaxel 225 mg/m^2 as a 3-hour infusion with carboplatin area under the curve (AUC) 6, and iii) paclitaxel 135 mg/m^2 as a 24-hour infusion with cisplatin 75 mg/m^2. However, there have been few direct comparisons of different doses and schedules for taxane-based combinations, and firm recommendations regarding optimal doses and schedules cannot be made at this time. Whether a weekly administration schedule of docetaxel or paclitaxel is associated with less toxicity than a three-weekly schedule remains to be determined.
- In patients for whom combination chemotherapy is inappropriate, single-agent taxane therapy is acceptable treatment.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are supported by randomized trials.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of taxanes in first-line therapy of advanced non-small cell lung cancer

POTENTIAL HARMS

- There were two randomized trials that compared best supportive care alone with best supportive care and either single-agent paclitaxel or single-agent docetaxel. Toxicity was generally higher with chemotherapy, although best supportive care was associated with more pulmonary symptoms, pain, and neurocortical adverse events than docetaxel.
- In a study comparing docetaxel-cisplatin and vinorelbine-cisplatin, toxicity was similar for cisplatin combined with either vinorelbine or docetaxel and docetaxel-carboplatin with the exception of anemia and nausea and vomiting, which were more common with vinorelbine-cisplatin.
- In another study, compared to the reference regimen of paclitaxel-cisplatin, the incidence of thrombocytopenia, anemia, and renal toxicity was higher with gemcitabine-cisplatin; hypersensitivity reactions were more common with docetaxel-cisplatin; and febrile neutropenia and nausea and vomiting were less frequent with paclitaxel-carboplatin.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- No study has directly compared paclitaxel-cisplatin with vinorelbine-cisplatin, the current Ontario standard regimen; however, in one randomized study, paclitaxel-cisplatin was comparable to docetaxel-cisplatin, gemcitabine-cisplatin, and paclitaxel-carboplatin with respect to response rates and survival.
- Taxane-carboplatin regimens may offer modestly inferior survival compared with taxane-cisplatin regimens; however, the toxicity profile of the carboplatin regimen is more attractive with respect to nausea and vomiting.
- Quality of life assessments were not reported in all trials, and there are some limitations in interpreting this subjective outcome in unblinded clinical trials. To date, no consistent quality of life benefits have been detected for paclitaxel-based chemotherapy regimens; however, one large trial suggested limited quality of life benefits in favour of docetaxel combined with either cisplatin or carboplatin over vinorelbine-cisplatin.
- Based on clinical experience and evidence from other cancer sites, it is the opinion of experts on the Lung Disease Site Group that retreatment of relapsed advanced non-small cell lung cancer with the first-line chemotherapy regimen is a reasonable option if that regimen initially induced clinically significant tumour regression that continued for at least three months from the completion of treatment.
- For logistical reasons, a three-hour paclitaxel administration is favoured over the 24-hour administration; docetaxel infusion time is only one hour. Three-hour paclitaxel regimens in combination with cisplatin or carboplatin are associated with a risk of significant neurotoxicity.
- Evidence regarding the substitution of gemcitabine for platinum with either docetaxel or paclitaxel is limited. The efficacy of these regimens appears to be comparable to cisplatin-based regimens. However, if cisplatin is contraindicated, there are more data relating to carboplatin as an alternative than to gemcitabine. Carboplatin with either docetaxel or paclitaxel has a similar efficacy to vinorelbine-cisplatin but a different toxicity profile. For the rare patients fit enough for combination chemotherapy, but for whom cisplatin and carboplatin are contraindicated, a taxane-gemcitabine combination may be considered.
- No evidence exists substantiating the use of taxane-based triplet combinations. These should not be used except in the context of a clinical trial.
- Care has been taken in the preparation of the information contained in this document. Nonetheless, any person seeking to apply or consult the practice guideline is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or warranties of any kind whatsoever regarding their content or use or application and disclaims any responsibility for their application or use in any way.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Lung Cancer Disease Site Group. Chu Q, Vincent M, Logan D, Mackay JA, Evans WK. The role of taxanes in first-line therapy of advanced non-small cell lung cancer [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2004 Jul 20. 49 p. (Practice guideline report; no. 7-7-1). [65 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 Jul 20

GUIDELINE DEVELOPER(S)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Practice Guidelines Initiative (PGI) is the main project of the Program in Evidence-based Care (PEBC), a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

SOURCE(S) OF FUNDING

Cancer Care Ontario
Ontario Ministry of Health and Long-Term Care

GUIDELINE COMMITTEE

Lung Cancer Disease Site Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

For a current list of past and present members, please see the Cancer Care Ontario Web site.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Members of the Lung Disease Site Group (DSG) disclosed potential conflict of interest information.

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GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- The role of taxanes in first-line therapy of advanced non-small cell lung cancer. Summary. Toronto (ON): Cancer Care Ontario (CCO). Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.
- Browman GP, Levine MN, Mohide EA, Hayward RSA, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. J Clin Oncol 1995;13(2):502-12.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on November 15, 2004. The information was verified by the guideline developer on December 13, 2004.

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